



*It is our responsibility as parents, scientists, regulators, and physicians to protect the smallest among us from environmental hazards.*

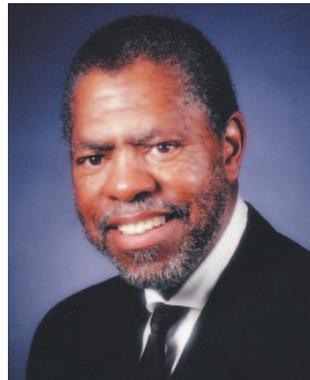
### Children's Health: A Mixed Review

Children are our most precious resource, so it is critical that they have the opportunity to develop into healthy and productive citizens. We can be proud of the fact that the health and safety of children is better than at any time in recorded history. Yet, the report card on the well-being of our children is a mixture of success and failure. The infant mortality rate is at a record low, but is still higher than in many countries. Academic achievement is up, but still lags behind many industrialized nations. Of the 60 million children younger than 15 years of age in the United States, more than 47,000 died in 1994 from preventable diseases (1,2). There have been sizable increases in chronic respiratory conditions, with asthma and chronic bronchitis increasing by 79% and 76%, respectively, from 1982 to 1993 (3). Seventeen percent of children in the United States are reported to have a developmental disability (4). The high rates of homicide, suicide, unintentional injury, poverty, violence, alcohol and tobacco use, asthma, autism, and developmental and behavioral disorders suggest that many challenges remain.

The environment in which we raise our children is dramatically different from that of a few generations ago. Intensive use of pesticides, dependence on automobiles, a regular regime of vaccinations, new consumer products, highly refined foods and beverages, and a steady diet of television and computer games are but some of the more obvious differences in our children's environment. All of these changes occurred in the past 50 years, creating an environment vastly different from that of the previous 100,000 years of human existence. At the same time that these changes have occurred, there has been an increase in reported cases of asthma, behavioral disorders such as autism and attention deficit/hyperactivity, and birth defects such as cryptorchidism. It is not too great a leap to wonder if the changes in our children's environment are responsible for some of their health problems.

There is ample evidence that children are often more vulnerable than adults to environmental agents. Epidemiologic studies show reduced lung capacity in children living in areas with high levels of air pollution (5,6). Studies by Needleman (7,8) demonstrated a clear association between low blood lead levels in children and reduced intelligence and greater aggressiveness (7,8). Children born to women engaged in farming have an increased risk of cryptorchidism (9). Recent epidemiologic studies suggest an association between nitrate levels in drinking water and risk of juvenile diabetes (10). Even otitis media, the ear infection that plagues 80% of American children, was shown in a small study among Inuit infants to have a possible association with prenatal organochlorine exposures (11).

There are too many holes in the children's environmental health and safety net. In most instances, we lack adequate information to determine which are the most significant health problems and what should be done about them. It has been estimated that less than 3% of the total federal research enterprise is devoted to children's health, even though the 80 million children (individuals younger than 21 years of age) represent 30% of the U.S. population (12). This raises two important questions: a) Are federal investments related to chil-



drren's health consistent with investments in other areas? and b) Is it adequate to generate the information needed to inform public health decision making?

Attempts are being made to improve the situation. One major initiative is the President's Executive Order on children's environmental health and safety (13). In response to this order, the President's Task Force on Environmental Health Risks and Safety Risks in Children was created with joint leadership between the Department of Health and Human Services and the Environmental Protection Agency (EPA). Through this group, a better orchestrated research agenda should evolve around many of the important questions in children's environmental health, such as:

- Do current models of hazard identification capture the agents of concern to children?
- Is there adequate data on *in utero*, perinatal, and childhood exposure?
- Are exposure studies appropriate for modeling exposure of children based on their biology, behavior, and activities?
- Do we have adequate knowledge of dose response and mechanisms to assess risk in infants and children?
- Do we have adequate information on timing of exposure; that is, do exposures earlier in life have the same health consequences as exposures later in life?

The NIEHS and its federal partners have initiated a number of programs that address children's environmental health issues. We have teamed with the EPA and the Centers for Disease Control and Prevention (CDC) to develop the first federal Children's Environmental Health and Disease Prevention Centers. At present, there are eight centers that focus on respiratory diseases and asthma, neurodevelopmental impairment, pesticide poisoning, and diseases resulting from exposure to agricultural chemicals. Future plans call for developing more centers devoted to studying the neurodevelopmental and neurobehavioral effects of environmental exposures in children.

Asthma remains a major childhood problem, particularly among minorities, and has received much attention from the federal research community. The National Institute of Allergy and Infectious Diseases (NIAID) has an ongoing Inner-City Asthma study in which NIEHS plays a role. NIAID and the NIEHS together are evaluating intervention studies aimed at reducing incidence of asthma attacks by reducing levels of airway allergens such as those from cockroaches and dust mites. NIAID and the NIEHS, together with the EPA, also are evaluating the relationship of indoor and outdoor particulate matter and other pollutants to asthma severity. The NIEHS has also teamed with the Department of Housing and Urban Development to do a National Allergen Survey that will identify the most common

household allergens in our homes. In addition, the National Heart, Lung, and Blood Institute supports several research activities to identify the causes of asthma in children and to identify potential approaches to prevention by investigating the complex interactions involved in exposure during infancy to respiratory infections and environmental allergens and irritants, lung development, and inherited predispositions to allergy. This information will help guide future research and remediation efforts.

The NIEHS is also supporting a number of studies investigating environmental endocrine disruptors. Endocrine disruptors are a diverse group of compounds that include plasticizers, polychlorinated biphenyls, many pesticides, and dioxins. These compounds are so pervasive that studies have shown them to appear in 95% of the U.S. population (14). The concern is that when exposure occurs very early in life, these compounds have the potential to disrupt critical endocrine pathways with potential future effects on reproductive, neurologic, and immunologic systems. This possibility has been verified in NIEHS studies in rodents which showed that early exposure to some pesticides resulted in reproductive, neurologic, and immunologic deficits later in life. These and other studies on the effects of early exposure to endocrine disruptors continue. Additionally, we have teamed with the CDC to assess what the actual, real-world exposures to endocrine disruptors are in a representative U.S. population. Results of this exposure assessment study will help guide us in selecting compounds for future study.

We are greatly interested in the potential of birth registries and prospective cohorts to decipher the genetic and environmental contributions to many diseases. We have already joined with the Norwegian government on a study of cleft palate, a common birth defect. Norway has one of the highest reported rates of cleft palate in the world, as well as a highly organized birth registry that records these defects. For this study, both genetic samples and data on environmental exposures of mothers and infants are being collected. When completed, this study will provide the largest and most comprehensive collection of data ever obtained on the genetic and environmental components of this birth defect.

The NIEHS also hopes to build on plans currently under way in Norway to recruit 100,000 pregnant women and their children. These families would be followed in a lifetime cohort study of health. The NIEHS is investigating the possibility of collecting and storing blood and urine samples from these women to assess environmental and other exposures during pregnancy. This information on exposures of the fetus would be used to study the effects of environmental factors during this crucial period on birth defects, developmental problems, childhood diseases, and even diseases of adulthood.

The Norwegian Birth Registry offers an excellent opportunity to gain insight into genetic and environmental components of children's health with a relatively modest investment. However, this study will be unable to fully capture the exposures and genetic diversity of the U.S. population. There is a great deal of federal interest in creating a U.S. birth cohort—the National Longitudinal Study of Environmental Influences on Child Health—that could be tracked over an entire lifespan and assessed for genetic and environmental contributors of disease. The sample size, as well as monitoring expenses, might well prevent such a cohort from being developed in this country. Nevertheless, the possibility of such a study is being actively discussed by the agencies participating in the President's Task Force on Environmental Health Risks and Safety Risks in Children.

A national twin registry offers another outstanding mechanism for determining the relative contributions of genes and environment in disease development, both in childhood and in adulthood. A number of studies have already demonstrated the value of comparing disease rates in monozygotic versus dizygotic twins. For example, autism, attention deficit/hyperactivity disorder, and multiple sclerosis occur

more frequently in identical twins than in fraternal twins, suggesting an underlying genetic susceptibility in these disorders (15–17). In the case of late-onset Parkinson disease, however, there is no difference in rates between identical and fraternal twins, suggesting that environmental components may play a major role in this disease (18). Such comparisons can help guide the research agenda so that the most promising avenues are pursued. There are already several regional twin registries (Mid-Atlantic Twin Registry, Missouri, Minnesota, Pennsylvania), as well as twin registries of people in the armed forces. What is needed, however, is a more uniform system that could cover the entire U.S. population. Again, such a registry would be an expensive proposition, but one in which the knowledge gained would benefit medical practice many fold over the original investment.

It is our responsibility as parents, scientists, regulators, and physicians to protect the smallest among us from environmental hazards. What is lacking is not the will, but the knowledge. Yet, as is obvious, identifying the environmental contributors to childhood disease is beyond the resources of any single organization. Creative partnerships and collaborations are necessary for many of the more significant research advances in this area. Given the importance of children for our nation's future, it is only prudent that we make the investments and forge the partnerships that will be critical in establishing a national research program on children's environmental health.

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